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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/477,082	12/30/99	KIDD V	2427/IE988-U

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EXAMINER	
HUNT, J	
ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 10/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/477,082	Kidd et al.
Examiner	**Art Unit**
Jennifer Hunt	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above, claim(s) *21-25 and 30-47* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-20 and 26-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicant's preliminary amendment filed 4/10/2001. The amendment has ben entered as paper #10.

Election/Restriction

2. Applicant's election with traverse of Group I, claims 1-20 and 26-29, and the species "nucleic acid detection" in Paper No. 12 is acknowledged. The traversal is on the ground(s) that there is no undue search burden because the inventions of Groups I, II, and V are classified in the same search class, and III and IV are in the same subclass as well. Applicant further argues that the groups share unifying features. This is not found persuasive because although the searches are overlapping, they are not coextensive. A search for one Group would not be sufficient for a search of any other group. The mere fact that Groups contain similar subject matter does not indicate that search and consideration are identical. Thus for reason set forth in the previous office action, because the Groups have different classifications and require distinct searches, the restriction is maintained.

Upon further consideration, the species requirement has been withdrawn, and the search includes both protein and nucleic acid detection.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-47 are pending in the application. Claims 21-25 and 30-47 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1-20 and 26-29 are considered herein.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 10-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "poor prognosis" in claim 10 is a relative term which renders the claim indefinite. The term "poor prognosis" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of a "poor prognosis" cannot be determined, and thus it is not clear what would be considered a "poor prognosis" and what would not. Dependent claims 11-20 fail to correct this deficiency.

Claim Rejections - 35 U.S.C. § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

7. Claims 1, 6-8, and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Mandruzzato et al., J. Exp. Med., Vol. 186, No. 5, pages 785-793, August 29, 1997, (IDS).

Mandruzzato et al. teaches a method of diagnosis or prognosis of a cancer (Head and Neck Cancer) by detecting inactivation of a CASP8 gene by detecting modification of CASP8 genomic DNA. The mutation detected includes a deletion (see abstract and page 789, last paragraph, bridging to page 790) .

8. Claims 1-3, 6-10, 13-14, 17-20, and 26-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Hunter et al., US Patent 6,172,190, January 9, 2001.

US 6,172,190 teaches a method of diagnosis or prognosis of a cancer (a disorder associated with apoptotic cell death) by detecting inactivation of a CASP8 gene by detecting modification of CASP8 genomic DNA (which would include deletions). '190 also teaches

methods of detection of CASP8 inactivation by detecting the lack of a CASP8 protein using an immunoassay (western blot) or detecting a modification of DNA using a labeled nucleic acid probe, including oligonucleotide PCR primers which have at least 15 bases which specifically hybridize to CASP8 and the corresponding diagnostic kits (see for example column 5, lines 15-40, column 7, lines 52-column 8, line 4, column 9, lines 17-32, column 10, lines 16-40, column 13, line 56-column 14, line 9, and column 18, lines 12-20).

Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-3, 6-10, 13-14, 17-20, and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mandruzzato et al., J. Exp. Med., Vol. 186, No. 5, pages 785-793, August 29, 1997, (IDS), in view of Hunter et al., US Patent 6,172,190, January 9, 2001 or Dixit et al. WO 97/46662, published December 11, 1997 (IDS).

Mandruzzato et al. teaches a method of diagnosis or prognosis of a cancer (Head and Neck Cancer) by detecting inactivation of a CASP8 gene by detecting modification of CASP8

genomic DNA. The mutation detected includes a deletion (see abstract and page 789, last paragraph, bridging to page 790).

Mandruzzato et al. fails to teach detection of CASP8 gene modification using nucleic acid primers, detection by immunoassay, or the corresponding kits.

US 6,172,190 teaches a method of diagnosis or prognosis of a cancer (a disorder associated with apoptotic cell death) by detecting inactivation of a CASP8 gene by detecting modification of CASP8 genomic DNA (which would include deletions). '190 also teaches methods of detection of CASP8 inactivation by detecting the lack of a CASP8 protein using an immunoassay (western blot) or detecting a modification of DNA using a labeled nucleic acid probe, including oligonucleotide PCR primers which have at least 15 bases which specifically hybridize to CASP8 and the corresponding diagnostic kits (see for example column 5, lines 15-40, column 7, lines 52-column 8, line 4, column 9, lines 17-32, column 10, lines 16-40, column 13, line 56-column 14, line 9, and column 18, lines 12-20).

WO 97/46662 teaches methods of determining a gene mutation, including detecting a protein (or lack thereof) using immunoassay, and also detecting mutation using PCR and nucleic acid probe methods(see pages 45-55) .

Therefor it would have been *prima facie* obvious to one of ordinary skill in the art to use the methods of determination of gene inactivation taught in US Patent 6,172,190 or WO 97/46662, to detect modifications of the CASP8 gene taught in Mandruzzato et al., and one

would have been motivated to do so because other mutations of CASP-8 are likely and would be helpful in tumor studies, as taught in Mandruzzato et al. (see page 791).

11. Claims 1, 4-6, and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mandruzzato et al., J. Exp. Med., Vol. 186, No. 5, pages 785-793, August 29, 1997, (IDS), in view of Herman et al. (1), PNAS, Vol. 93, pages 9821-9826, September 1996, or Herman et al. (2), PNAS, Vol. 91, pages 9700-9704, October 1994.

Mandruzzato et al. teaches a method of diagnosis or prognosis of a cancer (Head and Neck Cancer) by detecting inactivation of a CASP8 gene by detecting modification of CASP8 genomic DNA. The mutation detected includes a deletion (see abstract and page 789, last paragraph, bridging to page 790).

Mandruzzato et al. fails to teach detection of the specific CASP8 gene modification methylation of CASP8 promoter, using methylation polymerase chain reaction (PCR) assay.

Herman et al. (1) teaches that aberrant methylation, including promoter methylation is a common mutation in tumor suppressor genes in human cancers (see page 9821, first column). Herman et al. (1) also teaches the method of using methylation polymerase chain reaction (PCR) assay to detect promoter methylation mutations (see entire paper).

Herman et al. (2) teaches that aberrant methylation in regulator regions (which would include promoters) a common mutation in tumor suppressor genes in human cancers (see page 9700, first column).

Therefor it would have been *prima facie* obvious to one of ordinary skill in the art to use the methods of detection of promoter methylation taught and discussed in Herman et al. (1) and (2) to detect modifications of the CASP8 gene taught in Mandruzzato et al., and one would have been motivated to do so because other mutations of CASP-8 are likely and would be helpful in tumor studies, as taught in Mandruzzato et al. (see page 791).

12. Claims 1-10, 13-20, and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mandruzzato et al., J. Exp. Med., Vol. 186, No. 5, pages 785-793, August 29, 1997, (IDS), in view of Hunter et al., US Patent 6,172,190, January 9, 2001, or Dixit et al. WO 97/46662, published December 11, 1997 (IDS), and further in view of Herman et al. (1), PNAS, Vol. 93, pages 9821-9826, September 1996, or Herman et al. (2), PNAS, Vol. 91, pages 9700-9704, October 1994.

Mandruzzato et al. teaches a method of diagnosis or prognosis of a cancer (Head and Neck Cancer) by detecting inactivation of a CASP8 gene by detecting modification of CASP8 genomic DNA. The mutation detected includes a deletion (see abstract and page 789, last paragraph, bridging to page 790).

Mandruzzato et al. fails to teach detection of CASP8 gene modification using nucleic acid primers, detection by immunoassay, or the corresponding kits, or detection of the specific CASP8 gene modification methylation of CASP8 promoter, using methylation polymerase chain reaction (PCR) assay.

US 6,172,190 teaches a method of diagnosis or prognosis of a cancer (a disorder associated with apoptotic cell death) by detecting inactivation of a CASP8 gene by detecting modification of CASP8 genomic DNA (which would include deletions). '190 also teaches methods of detection of CASP8 inactivation by detecting the lack of a CASP8 protein using an immunoassay (western blot) or detecting a modification of DNA using a labeled nucleic acid probe, including oligonucleotide PCR primers which have at least 15 bases which specifically hybridize to CASP8 and the corresponding diagnostic kits (see for example column 5, lines 15-40, column 7, lines 52-column 8, line 4, column 9, lines 17-32, column 10, lines 16-40, column 13, line 56-column 14, line 9, and column 18, lines 12-20).

WO 97/46662 teaches methods of determining a gene mutation, including detecting a protein (or lack thereof) using immunoassay, and also detecting mutation using PCR and nucleic acid probe methods(see pages 45-55) .

Herman et al. (1) teaches that aberrant methylation, including promoter methylation is a common mutation in tumor suppressor genes in human cancers (see page 9821, first column). Herman et al. (1) also teaches the method of using methylation polymerase chain reaction (PCR) assay to detect promoter methylation mutations (see entire paper).

Herman et al. (2) teaches that aberrant methylation in regulator regions (which would include promoters) a common mutation in tumor suppressor genes in human cancers (see page 9700, first column).

Therefor it would have been *prima facie* obvious to one of ordinary skill in the art to use the methods of determination of gene inactivation taught in US Patent 6,172,190, or to use the methods of detection of promoter methylation taught and discussed in Herman et al. (1) and (2) to detect modifications of the CASP8 gene taught in Mandruzzato et al., and one would have been motivated to do so because other mutations of CASP-8 are likely and would be helpful in tumor studies, as taught in Mandruzzato et al. (see page 791).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Hunt, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that

sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Jennifer Hunt

October 22, 2001

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